SUPPORT FOR THE AMENDMENTS

Applicants have amended Claim 16 to change:

"wherein the ratio of HFA 227:HFA 134a ranges from 10:90 to 90:10 and said ratio is selected to produce aerosol particles having an MMAD (mass median aerodynamic diameter) greater that 2μm, wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm;

wherein said aerosol particles have an MMAD greater that 2 μm, and

wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm."

to

"wherein the ratio of HFA 227:HFA 134a ranges from 10:90 to 90:10;

wherein said aerosol is composed of particles which have a mass median aerodynamic diameter greater that 2 μm,

wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm, and

wherein said one or more active materials is at least one member selected from the group consisting of salbutamol, salts of salbutamol, beclometasone dipropionate, ipratropium bromide, and combinations thereof."

Support for this amendment can be found in Claim 16, as previously presented, and on page 13, lines 8-14, of the present specification.

Applicants have also added new Claims 34-48. Support for new Claims 34-36, 38-40, 42-44, and 46-48 can be found on page 13, lines 8-14, of the present specification. Support for new Clams 37, 41, and 45 can be found on page 12, line 26, to page 13, line 3, of the specification.

No new matter has been added. Claims 16, 17 and 34-48 are active in this application.

REMARKS

At the outset, Applicants' representative wishes to thank Examiner Alstrum Acevedo for the helpful and courteous discussion held with him on October 31, 2007, during which the prosecution of the above-identified application was materially advanced. The following remarks will expand and summarize the issues dicussed.

Present Claims 16, 17, and 34-48 relate to aerosols,

which are produced from a solution consisting of:

one or more solubilized active material(s),

a propellant consisting of a mixture of HFA 227 and HFA 134a, and ethanol as a cosolvent;

wherein the ratio of HFA 227:HFA 134a ranges from 10:90 to 90:10;

wherein said aerosol is composed of particles which have a mass median aerodynamic diameter greater that 2 μm,

wherein at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm, and

wherein said one or more active materials is at least one member selected from the group consisting of salbutamol, salts of salbutamol, beclometasone dipropionate, ipratropium bromide, and combinations thereof.

The inventors have discovered that the present aerosols are particularly effective for delivering substances to the respiratory tract. The cited reference neither discloses nor suggests the presently claimed aerosols or the benefits provided thereby. Accordingly, this reference cannot affect the patentability of the present claims.

The rejection of Claims 16, 17, 29, and 31-33 under 35 U.S.C. 102(b) in view of U.S. Patent No. 5,653,961 (McNally et al.) is respectfully traversed. At the outset, it is noted that McNally et al. only discloses compositions which contain butixcort. In contrast Claim 16, as currently amended, requires the presence of "one or more active materials" which 'is at least one member selected from the group consisting of salbutamol, salts of salbutamol, beclometasone dipropionate, ipratropium bromide, and combinations thereof."

There is nothing in McNally et al. which would even remotely suggest an aerosol which contains an active material selected from the group consisting of salbutamol, salts of salbutamol, beclometasone dipropionate, ipratropium bromide, and combinations thereof. In fact, a search of the electronic version of McNally et al. on the PTO's website reveals that the words "salbutamol," "beclometasone," and "ipratropium" do not appear in this reference.

Accordingly, present Claim 16, and the claims dependent thereon are not anticipated by McNally et al. Thus, the rejection of Claims 16, 17, 29, and 31-33 under 35 U.S.C. 102(b) as being anticipated by McNally et al. should be withdrawn.

Applicants further submit that there is nothing in McNally et al. which can make the present claims obvious. In particular, there is nothing in this reference which would suggest an aerosol in which at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm.

In this regard, it is noted that in the Office Action the position is taken that the disclosure of a respirable fraction of 45 % to 69 % in Examples 1 and 2 of McNally et al. implies the formation of an aerosol in which at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm. However, as explained during the above-noted discussion, the disclosure of such respirable fractions in Examples 1 and 2 of McNally et al. does not mean that such aerosols would necessarily meet the requirement that at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm.

In further support of this position, the Examiner's attention is directed toward the executed Declaration under 37 C.F.R. § 1.132 of Brambilla ("Declaration of Brambilla") filed herewith. The Examiner's attention is directed toward Mr. Brambilla's curriculum vitae, which is attached to his declaration and shows that he is the author of 20 scientific publications in the field of pressurized metered dose inhalers and a named inventor of 11 U.S. Patents in the field of pressurized metered dose inhalers.

As explained in the Declaration of Brambilla, the particle size distribution of aerosol particles is usually represented by a lognormal (Gaussian) distribution, which is, in turn, described by the mass median aerodynamic diameter (MMAD), which corresponds to the diameter of 50 % by weight of the particles, and by a geometric standard deviation (GSD). In contrast to arithmetic standard deviation, GSD is not a quantity but a factor. Powers of the geometric standard deviation are multiplied by (or divided into) the geometric mean to determine the set of values that lie within a given range of dispersion.

The respirable fraction of an aerosol is the percent by weight of particles having an aerodynamic particle size of less than 4.7 μm and is calculated as the ratio of the fine particle dose, *i.e.* the dose collected in the stages S3-Filter, and the mean emitted dose. Thus, 4.7 μm is only a cut-off value, and the particles collected in the stages S3-Filter could have a different distribution.

Accordingly, the MMAD and the respirable fraction are two distinct parameters, which are not directly correlated. As a consequence, an aerosol which has a respirable fraction comprised between 45% and 69% does not necessarily have a MMAD greater than 2 μm.

In fact, as shown in the two charts reported in Figure 3, on page 294 of B. Olsson, et al., PharmaEuropa, vol. 8, N. 2, pp. 291-298, June 1996 (Olsson et al.), particles collected at various stages in which the particle diameter is less than 4.7 μm, show different particle

distributions. In the chart on the left-hand side of Figure 3, most particles are collected at the Filter stage and have a very fine particle size, whereas in the chart on the right-hand side most of particles are collected at Stages 3-5 and have a greater particle size.

Similarly, as shown in Table 1 on page 21 of WO 98/56349, an aerosol of beclomethasone in HFA 134a and 13.0 % ethanol has a respirable fraction of 52.7 % but a MMAD of 1.0. In this case, the respirable fraction was calculated as the ratio of the fine particle dose of 46.2 μg to the mean emitted dose of 87.6 μg (*see*, Olsson et al., left-hand col. of page 292).

Thus, the mere fact that McNally et al. discloses a respirable fraction of 45 % to 69 % in Examples 1 and 2 does not suggest the formation of an aerosol in which at least 40% of said aerosol is composed of fine particles having a diameter of less than 4.7μm.

For this reason, this reference cannot make the present claims obvious. Accordingly, the rejection should be withdrawn.

The rejection of Claims 28 and 30 under 35 U.S.C. 103(a) in view of McNally et al., and further in view of U.S. Patent No. 5,190,029 (Byron et al.) is respectfully traversed.

As explained above, McNally et al. cannot make the presently claimed aerosols obvious. Applicants respectfully submit that there is nothing in Byron et al. which can cure the basic deficiencies of McNally et al. In particular, Byron et al. also does not disclose or suggest aerosols having the physical characteristics of those of the invention, nor teach how to make such aerosols.

Accordingly, the rejection should be withdrawn as well.

The rejection of Claims 16, 17, and 28-33 under the judicially-created doctrine of obviousness-type double patenting in view of claims 1-12, 14 and 16-29 of U.S. Patent No. 6,713,047; the rejection of Claims 16, 17, and 30-32 under the judicially-created doctrine of obviousness-type double patenting in view of claims 1-14 and 22-24 of U.S. Patent No.

6,964,759; and the rejection of Claims 16, 17, and 28-32 under the judicially-created doctrine of obviousness-type double patenting in view of claims 11-44 of U.S. Patent No. 6,713,047 are all respectfully traversed. Applicants respectfully submit that there is nothing in any of the claims of the cited patents which would suggest the presently claimed aerosols. Accordingly, the rejections should be withdrawn.

The provisional rejection of Claims 16 and 17 under the judicially-created doctrine of obviousness-type double patenting in view of Claims 1, 4-7, and 13 of co-pending U.S. Patent Application Serial No. 10/505,679 is respectfully requested to be held in abeyance pending the identification of otherwise allowable subject matter.

The rejection of 28-30 under 35 U.S.C. § 112, second paragraph, has been obviated by the cancellation of these claims. Accordingly, the rejection is no longer tenable and should be withdrawn.

Applicants respectfully submit that the present application is now in condition for allowance, and early notification to that effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
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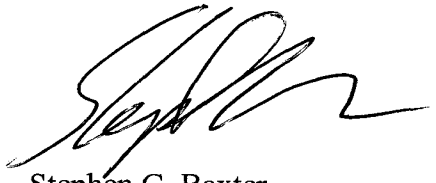

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